

Easy

Pathology

— Dr. Abdelrahman Khalifa —

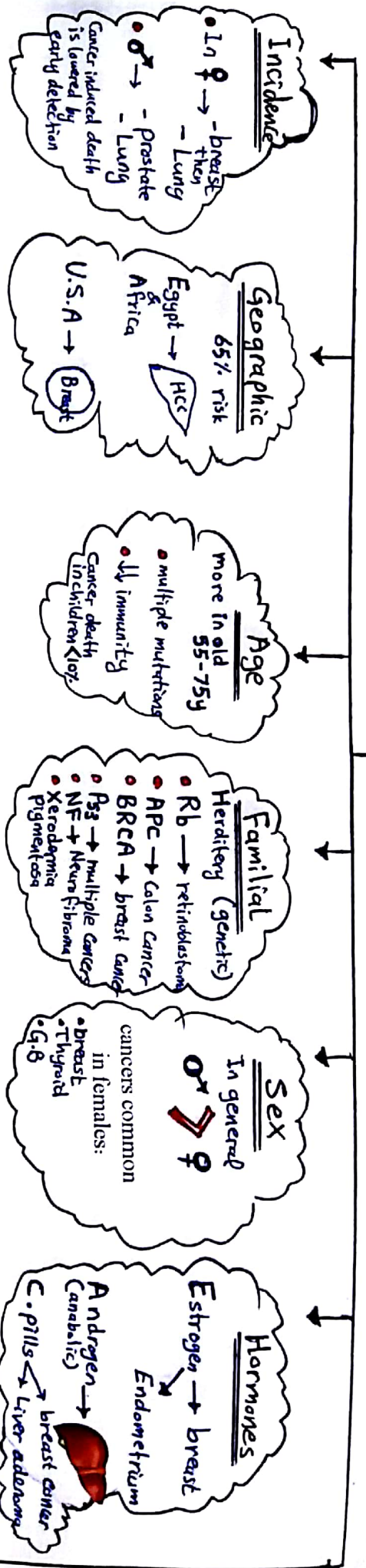
Neoplasm Carcinogenesis



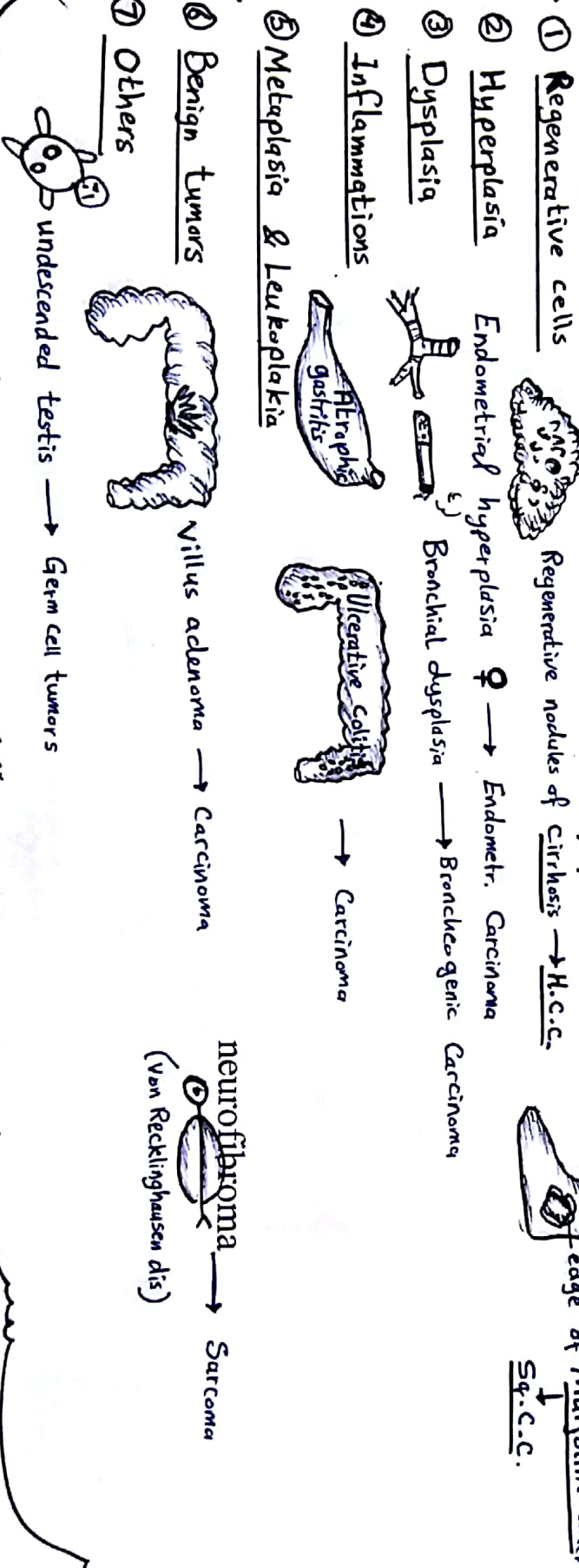
VISIT...

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Epidemiology & P.F.

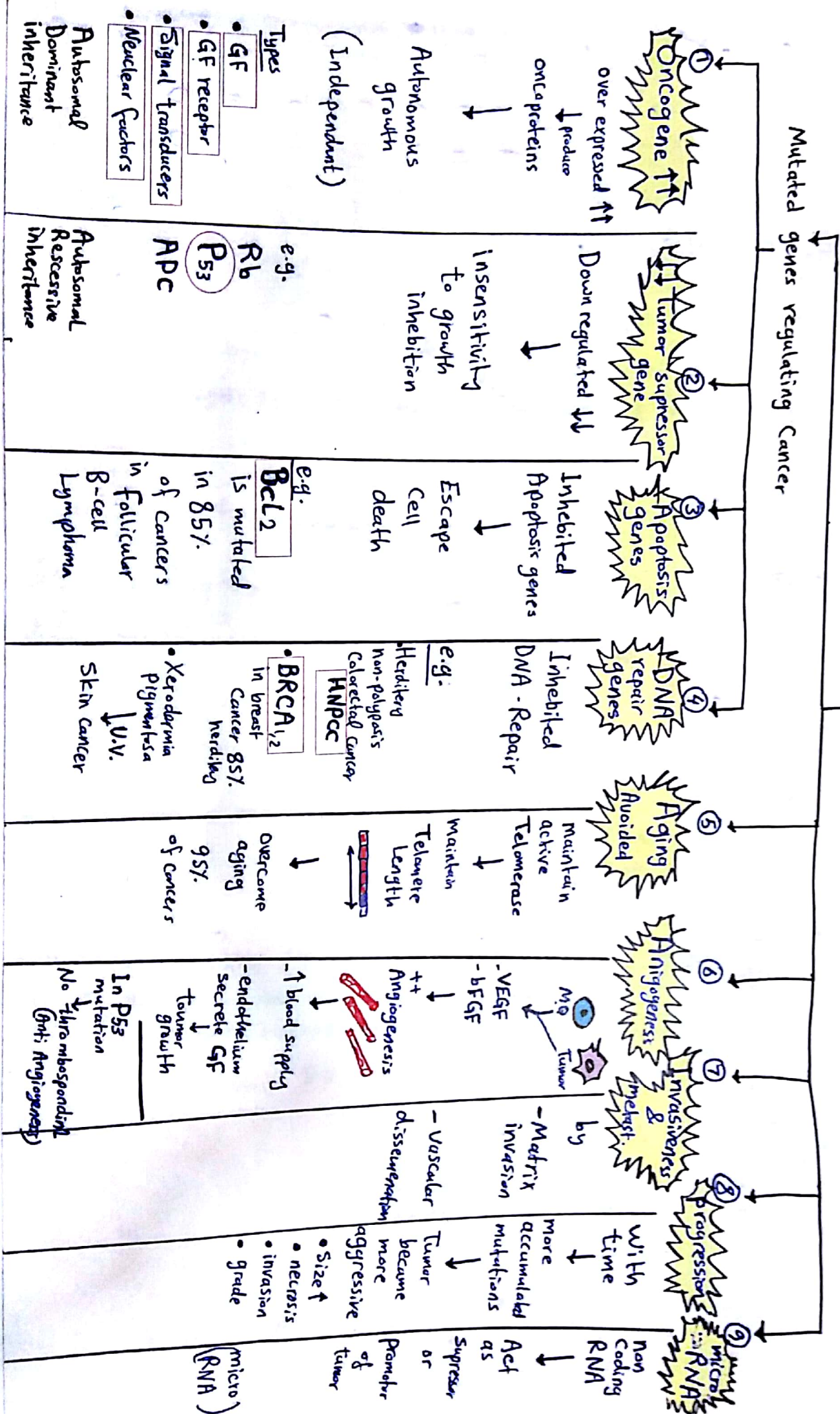


PreNeoplastic diseases (precancerous)



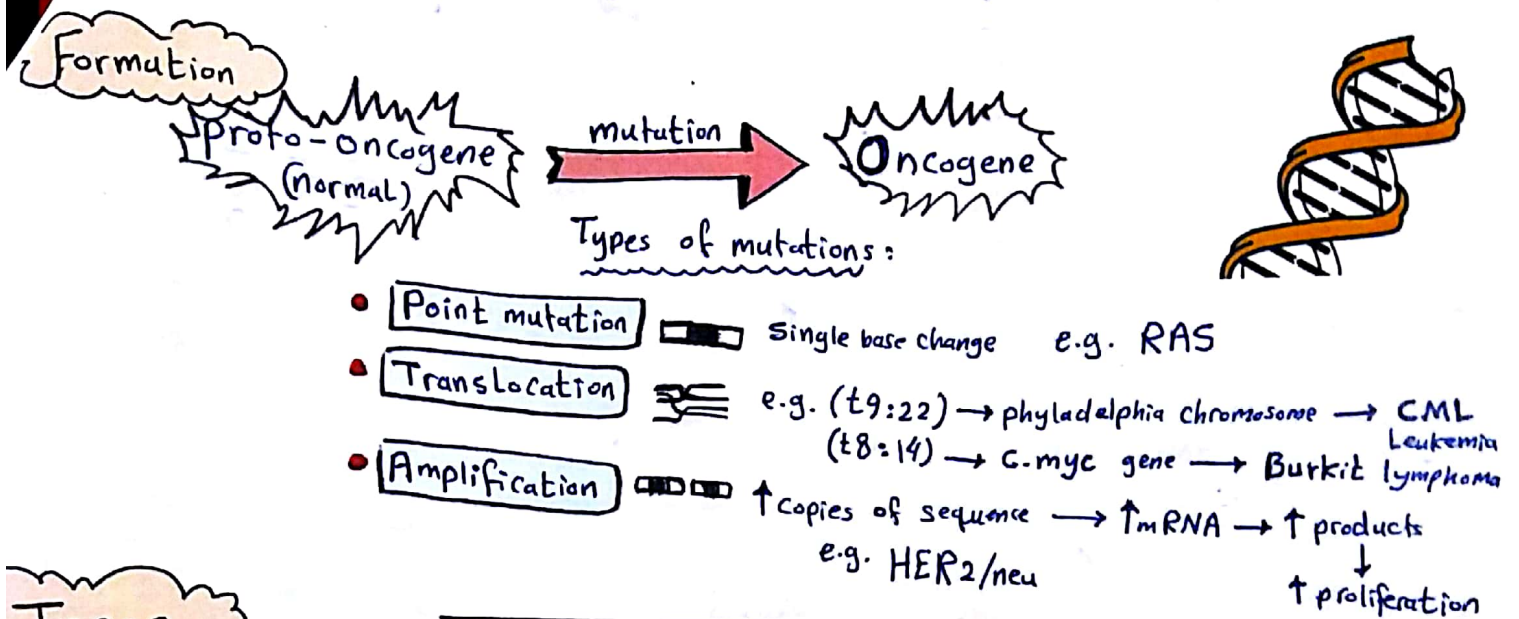
Molecular properties & Carcinogenesis

Tumor is multistep - multifactorial mutations of mono clonal cells to Acquire new properties



Oncogenes

A gene whose products (oncoproteins) are associated w/ tumor formation



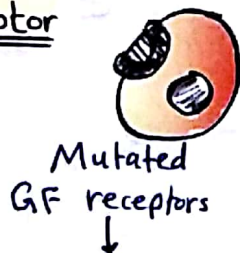
Types

① Growth Factor GF



e.g. **PDGF** in glioblastoma
TGF α in Sarcomas

② GF receptor



Mutated
GF receptors

Direct stimulation w/out G.F.s



Over expressed receptors

Increased sensitivity to G.F.s

e.g. **EGF-r (HER2/neu)**
in 30% of
Cancer
breast

③ Signal transduction

e.g. **RAS**

Activate signal pathway without GF or receptors



30% of human Cancer

④ Nuclear transcription



e.g. **MYC**

DNA transcription & enter S phase

c-myc in Burkitt's Lymphoma

⑤ Cell cycle regulatory proteins



In normal cell **Cyclins** $\rightarrow$ ++ **CDK** $\rightarrow$ Cell cycle progression

e.g. Some tumors produce Cyclin D e.g. **Mantle Lymphoma**
Cyclin dependant kinase **CDK4** in **Melanoma**

Tumor suppressor



Tumor suppressor genes are inhibited by

* Autosomal Recessive loss of one copy then acquired loss of the other copy

* Sporadic cases : loss of both copies is acquired

Rb

Control G1 to S check point

If inhibited (e.g. HPV) → bypass check point

P53

in 70% of tumors → mutated

In normal cell monitors stress (e.g. hypoxia) → Activate DNA repair gene

Cell death
يعتبر موتاً

activates apoptosis gene

In Case of failure



يا غير عيبه فل
يا غنوت اصنا الكل

e.g. P53 mutation by DNA virus proteins

HPV
HBV
EBV

APC

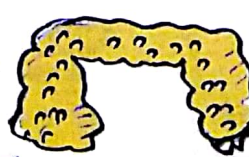
in 70% of sporadic Cancer Colon

* Normal APC → inhibits β Catenin

* In tumor APC inhibited or Lost → Active β Catenin (nuclear factor)

Cancer Colon

Adenomatous Polyps Coli
(hundreds of polyps)



Multistep Carcinogenesis

APC mutation

Hyperplasia of colon & Hundreds of Polyps (Adenoma)

K-RAS mutation

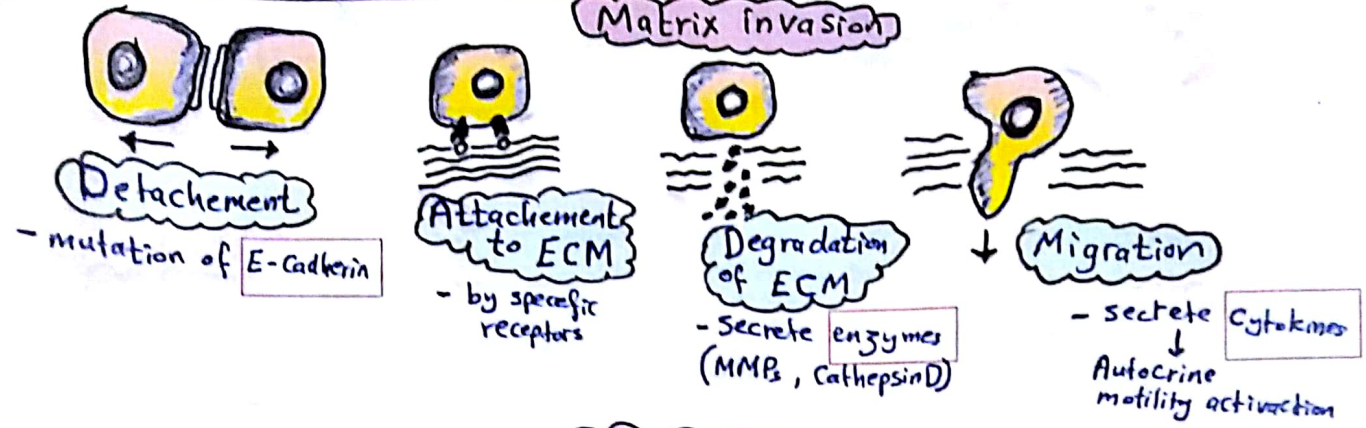
Advanced adenoma

Carcinoma

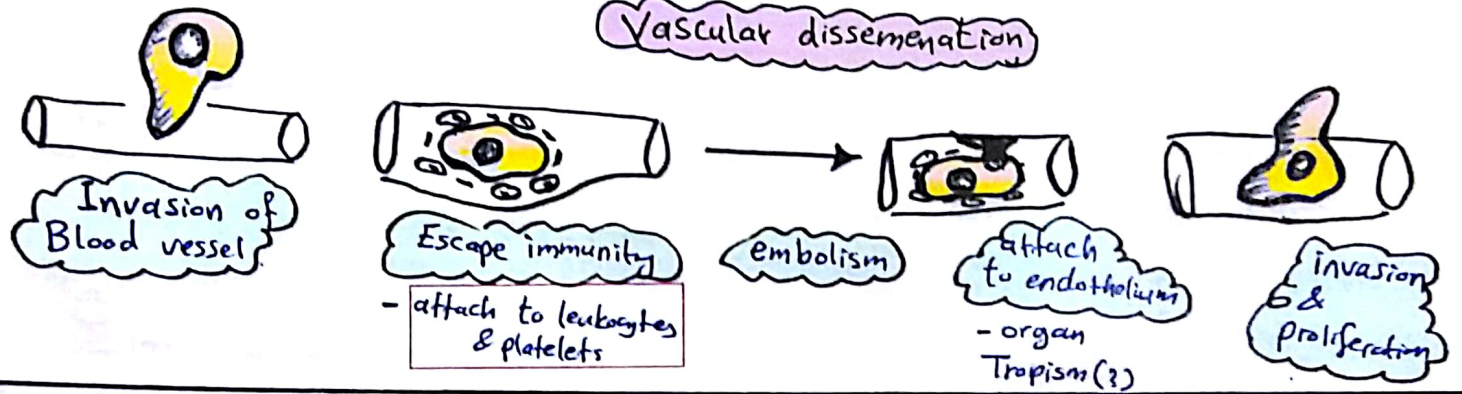
P53 mut.

Mechanism of invasion & metastasis

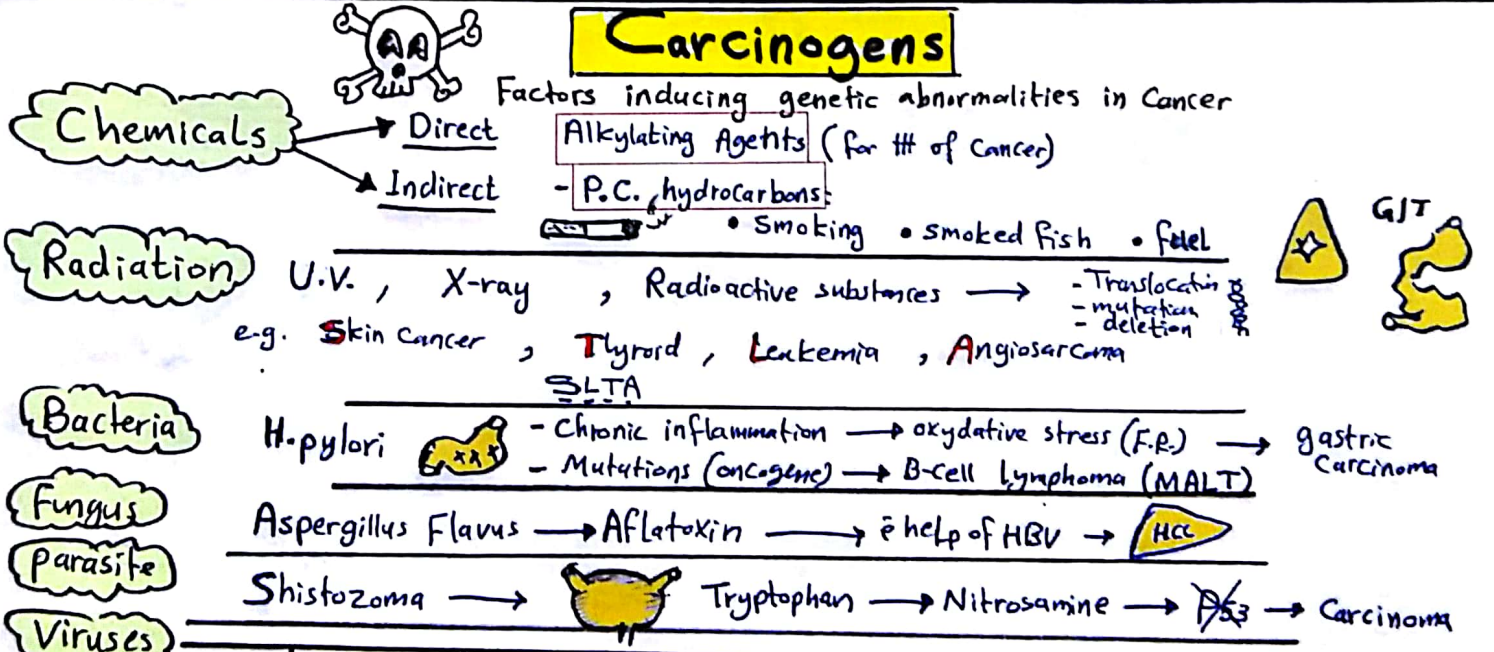
Matrix Invasion



Vascular dissemination



Carcinogens



HTLV-1 (RNA)	HCV (RNA)	HPV (DNA)	EBV (DNA)	HHV8 (DNA)	HBV (DNA)
- sexual trans. - milk	Similar to HBV	Type 16, 18, 31	- ↑ MYC - ↓ apoptosis	↓ AIDS Kaposi Sarcoma	- chronic inflammation F.R. - HBx protein (oncogene) signal transduction - ↓ Tumor sup. genes
↓ 1% CDK ↑ & P53 ↓ → leukemia after 20y	→ HCC	↓ P53 → ↓ Bax ↓ apoptosis CDK & cyclin ↓ Aging → Carcinoma of Cervix, vagina, oral, anal	→ B lymphoma Burkitt lymphoma Hodgkin lymphoma Nasopharyngeal carcinoma		→ H.C.C.

Clinical effects



Compression

e.g. pituitary adenoma → compress gland → ↓ function
 Leiomyoma → renal ischemia

Fever

- cytokine - infection - ulcer - hemorrhage
 e.g. H. Lymphoma

Obstruction

of tubular organs

Cachexia

loss of weight + weakness + Anemia

- ↑ metabolism
 - TNF & IL1 → ↓ appetite, ↓ fatty acids
 - muscle damaging factor

Hormonal secretion

e.g. adenoma or adenocarcinoma



Paraneoplastic Syndrome

10-15% of cancer

Symptoms not directly related to tumor or metastasis



Sq.c.c.
Lung

ACTH → Cushing
 ADH
 PTH related protein → ↑ Ca



RCC

Erythropoietin → polycythemia



pancreatic
prostatic

→ thrombogenic factors



Carcinoid

→ Serotonin, Bradykinin

Lab diagnosis of Cancer

* Excision biopsy

Surgical Adequate Specimen



* Frozen section

Rapid technique



* FNAC

Fine needle aspiration

& Cytology

From palpable tumors

- Fast
 - used in Cervix dysplasia



* Immunohistochemistry (IHC)

Tumor products

- diagnostic
 - prognostic

Cytokeratin in Carcinoma

Vimentin in Sarcoma

LCA in Lymphoma

PSA in prostate

Er & Pr in breast

HER2/neu breast

* Flow cytometry

Detect Ag for phenotyping (Lymphoma)

* Tumor markers

detected in blood or tissue

PSA, CEA in colorectal & pancreatic ca
 AFP in HCC & yolk sac tumor

* Molecular (DNA)

For hereditary cancer & diagnosis